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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,169	06/22/2001	Aimee Dymphne Catherine Paulussen	JAB-1462	9249

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,169	PAULUSSEN ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *17-25 and 32-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0102*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a 371 of PCT/GB99/04380, filed December 22, 1999. It is noted that the International Search Report and International Preliminary Examination Report for PCT/GB99/04380 have been received and considered. The paper and computer readable forms of the Sequence Listing filed April 13, 2004 have been entered.

Election/Restrictions

2. Applicant's election without traverse of Group I, claims 1-16 and 26-31, in the reply filed on November 19, 2003 is acknowledged.

3. Claims 17-25 and 32-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 19, 2003.

Specification

4. The use of the trademarks RNEASY, SUPERSCRIPT, QIAAMP, QIAQUICK, BIGDYE, EXCELGEL, MULTIPHOR, TAQMAN, PRIMER EXPRESS, READY GEL, HYBOND, TWEEN, and X-OMAT has been noted in this application. Trademarks should be capitalized wherever they appear.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Drawings

5. The drawings are objected to because the drawings include a figure identified as Figure 9, as well as several separate figures identified as Figure 9a, 9b, etc. If the drawing identified as "Figure 9" is only part of the figure, it should be assigned a separate designation (e.g., be re-numbered as Figure 9a, with each subsequent subpart of the drawing being renumbered accordingly). The Brief Description of the Drawings should also be modified to reflect the renumbering of the figures.

Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-16 and 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3-7 are indefinite because it is unclear whether the claims are drawn to a method of "identifying subjects having a high or low drug metabolizing phenotype associated with cytochrome CYP3A5 expression," as set forth in the preamble of claim 1, or whether the claims are drawn to a method of "screening genomic DNA" from a subject for polymorphic variants, as required by the method step of the claims. The claims do not set forth how the screening of genomic DNA results in the "identifying" reciting in the claim preamble. Clarification is required.

Claims 1 and 3-7 are indefinite over the recitation of the limitation "said subject" in claim 1 because there is insufficient antecedent basis for this limitation in the claims.

Claims 1 and 3-7 are indefinite over the recitation of the language "screening...for the presence or absence of one or more polymorphic variants in a transcription regulatory region..." in claim 1, because it is unclear as to whether the claims actually require screening for different variant genes, or whether the claims are drawn to a method requiring screening for polymorphic variations within a region of a particular gene. Clarification is required.

Claims 1 and 3-7 are indefinite over the recitation of the phrase "characteristic of a high drug metabolizing phenotype" in claim 1, because it is unclear whether this

phrase refers back to CYP3A5 (i.e., that this is a property of CYP3A5, e.g., as compared to other CYP genes), or whether this recitation refers back to the recited "polymorphic variants" or "transcription regulatory region."

Claim 7 is indefinite over the recitation of the language "capable of hybridizing selectively." Capability is a latent characteristic, and it is unclear whether this language is intended to require that selective hybridization actually does occur during the practice of the claimed method, or whether this language merely refers to a property of the oligonucleotide molecules employed in the method (such that, e.g., under some type of conditions, those molecules would be "capable of selectively hybridizing"). Clarification is required.

Claim 7 is indefinite over the recitation of the limitation "the wild type or variant sequences" because there is insufficient antecedent basis for this language in the claim.

Claim 2 is indefinite because it is unclear whether the claim is drawn to a method of "screening human subjects for suitability for treatment with a drug metabolized by CYP3A5," as set forth in the preamble, or whether the claim is drawn to a method of "screening" for polymorphic variants, as required by the method step of the claim. The claim does not set forth how the screening method step results in or relates to the screening for suitability for drug treatment recited in the claim preamble. It is further noted that the claim does not indicate any relationship between the subjects of the preamble and the material screened during the practice of the method. Clarification is required.

Claim 2 is indefinite over the recitation of the language "screening for the presence or absence of one or more polymorphic variants in a transcription regulatory region…", because it is unclear as to whether the claim actually requires screening for different variant genes, or whether the claim is drawn to a method requiring screening for polymorphic variations within a region of a particular gene. Clarification is required.

Claim 2 is indefinite over the recitation of the phrase "characteristic of a high drug metabolizing phenotype", because it is unclear whether this phrase refers back to CYP3A5 (i.e., that this is a property of CYP3A5, e.g., as compared to other CYP genes), or whether this recitation refers back to the recited "polymorphic variants" or "transcription regulatory region."

Claims 8-16 are indefinite because it is unclear whether the claims are drawn to a method of "identifying one or more polymorphic variants in a transcription regulatory region of DNA encoding cytochrome CYP3A5," as set forth in the preamble of claim 8, or whether the claims are drawn to a method of subjecting amplified DNA to restriction digestion in order to detect the presence or absence of a mutation, as required by the final process step of the claims. The claims do not set forth how the digestion and mutation detection result in the "identifying" reciting in the claim preamble. Clarification is required.

Claims 8-16 are indefinite over the recitation of the limitations "the sample DNA," "the wild type," "said one or more variant sequences," "said amplified wild type or variant sequences," and "said mutation" in claim 8, because there is insufficient antecedent basis for these limitations in the claims.

Claims 8-16 are indefinite over the recitation of the language "capable of selectively hybridizing" in claim 8. Capability is a latent characteristic, and it is unclear whether this language is intended to require that selective hybridization actually does occur during the practice of the claimed method, or whether this language merely refers to a property of the oligonucleotide molecules employed in the method (such that, e.g., under some type of conditions, those molecules would be "capable of selectively hybridizing"). Further, as the claim refers to selectively hybridizing "to the wild type and/or said one or more variant sequences," it is unclear as to how the term "selectively" modified the recitation "hybridizing" within the context of the claimed invention. Clarification is required.

Claim 9 is indefinite over the recitation of the limitation "said molecule" because there is insufficient antecedent basis for this limitation in the claims.

Claims 10-16 are indefinite over the recitation of the limitation "said molecule" in claims 10, 11, and 14 because there is insufficient antecedent basis for this limitation in the claims.

Claims 26-31 are indefinite because it is unclear whether the claims are drawn to a method of "diagnosing susceptibility of an individual to a disease associated with environmental toxins or procarcinogens metabolized by CYP3A5," as set forth in the preamble of claim 26, or whether the claims are drawn to a method of screening for the presence or absence of a polymorphic variant, as required by the method step of the claims. The claims do not set forth how the screening step results in or relates to diagnosis. Clarification is required.

Claims 26-31 are indefinite over the recitation of the language "screening for the presence or absence of a polymorphic variant in a transcription regulatory region...", because it is unclear as to whether the claim actually requires screening for different variant genes, or whether the claim is drawn to a method requiring screening for polymorphic variations within a region of a particular gene. Clarification is required.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-6 and 26-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jounaidi et al (Biochem. Biophys. Res. Comm. 205(3):1741-1747 [12/1994]).

As is acknowledged at page 27 of Applicants' specification, Jounaidi et al disclose the screening of human genomic CYP3A5 nucleic acids and detection therein of the –475 and –147 polymorphisms of Applicants' invention (see also page 1742 and Figure 2 of Jounaidi et al). It is noted that claims 1-6 and 26-31 as written merely require such screening steps, as the claims do not actually include steps of identifying individuals as having a particular phenotype (see claim 1) or as being suitable for treatment (see claim 2), or steps of disease diagnosis (see claim 26). Accordingly, Jounaidi et al anticipate the claims as written.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 7-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jounaidi et al (Biochem. Biophys. Res. Comm. 205(3):1741-1747 [12/1994]) in view of Meyer (EP 0463395 A1 [1/1992]).

As is acknowledged at page 27 of Applicants' specification, Jounaidi et al disclose the screening of human genomic CYP3A5 nucleic acids and detection therein of the –475 and –147 polymorphisms of Applicants' invention (see also page 1742 and Figure 2 of Jounaidi et al). It is noted that the claims as written merely require, e.g., screening steps (claim 7) or steps of mutation detection (claims 8-16). Jounaidi et al do not disclose amplification of different gene variants using allele- or polymorphism-

specific primers, and further do not disclose the inclusion of restriction sites in such primers and detection of variants by restriction digestion, as required by the instant claims. Meyer discloses allele-specific amplification of different CYP gene variants corresponding to different drug-metabolizing phenotypes (see entire reference, particularly pages 4-7). Meyer further discloses differentiation of variants by restriction digestion of amplification products (see entire reference, particularly Figures 9-10). In view of the teachings of Meyer, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Jounaidi et al so as to have substituted therein the allele-specific amplification and restriction digestion methods of variant detection taught by Meyer for the sequencing steps taught by Jounaidi et al. Given the greater rapidity with which detection may be achieved using the steps of Meyer, an ordinary artisan would have been motivated to have made such a modification (including modification of primers so as to employ primers usable in differentiating the variants of Jounaidi et al by allele-specific amplification and digestion) for the advantages of increased speed and efficiency in achieving variant detection.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Primary Examiner
August 9, 2004